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Applicant (s): Shu Kobayashi et al.

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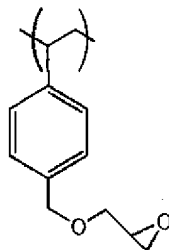
For: POLYMER INCARCERATED LEWIS ACID METAL CATALYST

DECLARATION OF RYO AKIYAMA

Ryo Akiyama declares as follows:

1. I am the same Ryo Akiyama who is named as an inventor in this application. I am also a co-author of the article "The Polymer Incarcerated Method for the Preparation of Highly Active Heterogeneous Palladium Catalysts", which was published in *JACS* 2003, 125, 3412-3413, and which has been cited as a reference against this application.
2. The Shu Kobayashi who is a coauthor on my *JACS* 2003 paper, and who is the inventor of US Patent No. 6,352,954, is the same Shu Kobayashi who is a coinventor in this application.
3. My native language is Japanese, but I can read and write English.
4. I am aware that the claims of this application have been rejected over my *JACS* 2003 article and over Dr. Kobayashi's US Patent No. 6,352,954. The purpose of this declaration is to provide information to the examiner in this application, in support of the patentability of my invention.

5. My JACS 2003 article describes polymers 1a, 1b and 1c, which were used to incarcerate palladium. Polymers 1a, 1b and 1c each contain 4-vinylbenzyl glycidyl ether units, which have this structure:

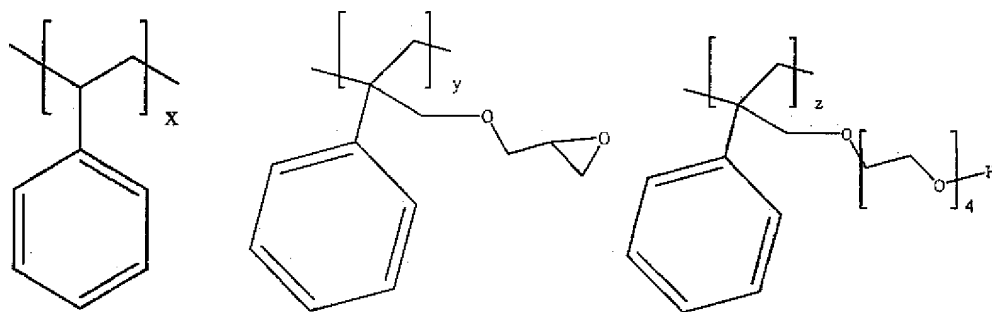


The 4-vinylbenzyl glycidyl ether units have a hydrophobic substituent (the aromatic ring), and a hydrophilic group (the glycidyl ether group) attached to the hydrophobic substituent. The glycidyl ether group also acts as a crosslinking group in polymers 1a, 1b and 1c. The glycidyl ether group is not linked directly to the main polymer chain.

6. In the invention that we are claiming in this application, we incarcerate a Lewis acid metal with a crosslinked polymer. The crosslinked polymer has hydrophilic substituents that contain crosslinking groups. These are linked directly to the main polymer chain. The crosslinked polymer also contains hydrophobic substituents, such as phenyl groups. These are also linked directly to the main polymer chain, but those hydrophobic substituents do not contain either hydrophilic groups or crosslinking groups. Therefore, the crosslinked polymer in this invention does not contain repeating units such as 4-vinylbenzyl glycidyl ether units, as I described in the JACS 2003 article.

7. I have found that the crosslinked polymer of this invention is better at incarcerating Lewis acid metals than the crosslinked polymers I described in the JACS 2003 article. To demonstrate this, experiments were run as described below.

8. Production Example 1 and Example 6 of this patent application accurately report actual experiments that were performed under my supervision and control. Production Example 1 describes the preparation of a copolymer of styrene, 2-[(2-phenylalloy) methyl]oxy and tetraethyleneglycol mono-2-phenyl-2-propenyl ether. The structure of the resulting copolymer is shown as chemical formula 4 in the patent application, and is repeated here. x, y and x have relative values of 91/5/4.



All of the repeating units of this copolymer have a hydrophobic substituent (the phenyl ring) bonded directly to the main polymer chain. None of the phenyl rings are substituted with either a hydrophilic group or a crosslinking group. In addition, the second and third repeating units shown in the structure each contains hydrophilic substituents containing crosslinking groups. Those hydrophilic substituents are linked directly to the main polymer chain. Example 6 of the patent application accurately describes the incarceration of scandium by this copolymer.

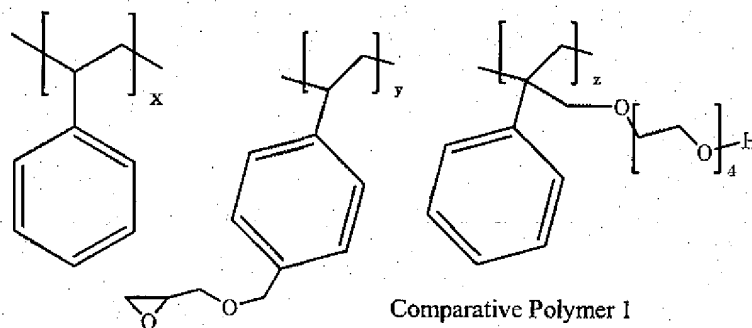
9. To compare with Example 6 of the patent application, scandium was incarcerated by two other copolymers, as described below. These are designated as Comparative Examples 1 and 2, respectively. All experiments and tests described below were run under my supervision and control.

10. Comparative Example 1: Glycidol (6.6 ml, 99.5 mmoles) was added to a suspension of 60% sodium hydride (4.00 g, 100 mmoles) in DMF (200 ml) at 0 °C and the mixture was agitated for 1 hour at room temperature. Next, 4-vinylbenzyl chloride (7.0 ml, 49.7 mmoles) and tetrabutylammonium iodide (1.84 g, 4.98 mmoles) were added at the same temperature, and the mixture was subsequently agitated for 5 hours at room temperature. The reaction mixture was cooled to 0 °C and subsequently diluted with diethyl ether, and the reaction was terminated by adding a saturated aqueous ammonium chloride solution. The aqueous layer was extracted several times with diethyl ether, and the organic layers were combined and dried using anhydrous sodium sulfate. The solvent was concentrated after filtration, and the residue was purified using silica gel chromatography (Hexane-AcOEt) to obtain 4-vinylbenzyl glycidyl ether (6.86 g, 73%). ^1H NMR (CDCl_3) δ =2.60 (d, 1H, J = 2.5 Hz, 5.1 Hz),

2.57 (d, 1H, $J = 4.2, 5.1$ Hz), 3.17 (dddd, 1H, $J = 2.7, 2.9, 5.1, 5.7$ Hz), 3.41 (dd, 1H, $J = 5.7, 11.3$ Hz), 3.75 (dd, 1H, $J = 2.9, 11.3$ Hz), 4.56 (dd, 2H, $J = 12.1, 22.8$ Hz), 5.23 (d, 1H, $J = 11.0$ Hz), 5.74 (d, 1H, $J = 17.6$ Hz), 6.70 (dd, 1H, $J = 11.0, 17.6$ Hz), 7.30 (d, 1H, $J = 8.8$ Hz), 7.38 (d, 1H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3) $\delta = 40.2, 50.7, 70.7, 72.9, 113.8, 126.2, 127.9, 136.4, 137.0, 137.4$.

Styrene (8.34 g, 80.1 mmol), 4-vinylbenzyl glycidyl ether (1.90 g, 9.99 mmol), tetraethylene glycol mono-2-phenyl-2-propenyl ether (3.10 g, 9.99 mmol) and AIBN (81.0 mg, 0.493 mmol) were dissolved in chloroform (12 ml) and heated and agitated in an argon atmosphere for thirteen hours under reflux conditions. The reaction mixture was poured into methanol (300 ml) upon cooling to solidify the polymer. The supernatant solution was removed by decantation, and the solids were dissolved in a small amount of tetrahydrofuran and poured into methanol again. The polymer precipitated was filtered and dried at room temperature under reduced pressure to obtain 7.31 g of a polymer (55% yield).

The polymer obtained had the structure shown below, and the composition ratio (x/y/z) of the individual monomer units was 84/10/6. The weight average molecular weight (M_w) was 36,937, the number average molecular weight (M_n) was 25,925 and the degree of dispersion (M_w/M_n) was 1.42. The polymer formed is henceforth referred to as Comparative Polymer 1.



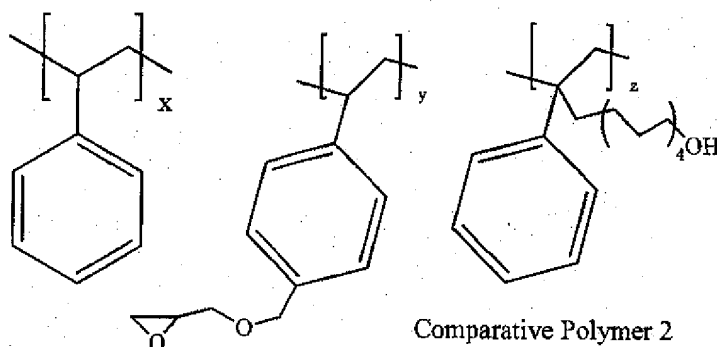
Comparative Polymer 1 (1.00 g) was dissolved in 20 mL of dichloromethane (DCM) at room temperature, and to this solution was added $\text{Sc}(\text{OTf})_3$ (200 mg, 0.406 mmol). The mixture was stirred for 15 min at this temperature. 20 mL of Hexane was slowly added to the mixture at room temperature. Coacervates were found to envelope $\text{Sc}(\text{OTf})_3$ in the media. The resulting catalyst capsules were collected by filtration after additional stirring for 30 min at room temperature and washed with hexane several times, then dried under

reduced pressure. Next, the collected capsules were left at 120 °C for 2 h under solvent-free conditions to cross-link the polymer chain. Finally, the cross-linked catalyst was washed with toluene and DCM several times, and dried at room temperature under reduced pressure to give Comparative Example 1 (1.20 g, 0.332 mmol/g of $\text{Sc}(\text{OTf})_3$ was loaded). The Sc leaching in all filtrates and washings was measured by XRF analysis to determine the catalyst loading.

11. Comparative Polymer 1 corresponds very closely to polymer 1c of my JACS 2003 article.

12. Comparative Example 2: Styrene (9.80 g, 87.2 mmol), 4-vinylbenzyl glycidyl ether (2.07 g, 10.9 mmol), 14-phenylpentadec-14-en-1-ol (3.30 g, 10.9 mmol) and AIBN (128.9 mg, 0.785 mmol) were dissolved in chloroform (13 ml), heated and agitated in an argon atmosphere under reflux conditions for 24 hours. The reaction mixture after cooling was poured into methanol (MeOH, 500 ml) to solidify the polymer. The product obtained was decanted to remove the supernatant solution, and the solids were subsequently dissolved in a small amount of tetrahydrofuran and again poured into methanol. The precipitated polymer was filtered and dried at room temperature under reduced pressure to obtain 6.95 g of a polymer (48% yield).

The polymer obtained had the structure shown below, and the composition ratio (x/y/z) of the individual monomer units was 79/11/10. The weight average molecular weight (M_w) was 23,843, the number average molecular weight (M_n) was 18,857 and the degree of dispersion (M_w/M_n) was 1.26. The polymer formed is henceforth referred to as Comparative Polymer 2.

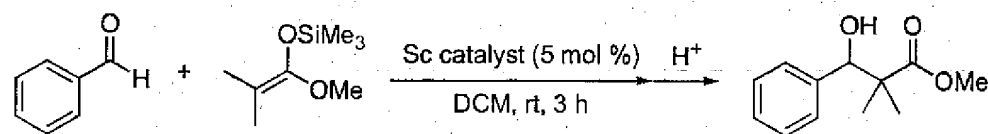


Comparative Polymer 2 (500 mg) was dissolved in 10 mL of DCM at room temperature, and to this solution was added $\text{Sc}(\text{OTf})_3$ (50 mg, 0.406 mmol). The mixture was stirred for 15 min at this temperature. 40 mL of Hexane was slowly added to the mixture at room temperature. Coacervates were found to envelope $\text{Sc}(\text{OTf})_3$ in the media. The resulting catalyst capsules were collected by filtration after additional stirring for 30 min at room temperature and washed with hexane several times, then dried under reduced pressure. Next, the collected capsules were left at 120 °C for 2 hours under solvent-free conditions to cross-link the polymer chain. Finally, the cross-linked catalyst was washed with DCM several times, and dried at 100 °C under reduced pressure to give Comparative Example 2 (527 mg, 0.195 mmol/g of $\text{Sc}(\text{OTf})_3$ was loaded). The Sc leaching in all filtrates and washings was measured by XRF analysis to determine the catalyst loading.

Comparative Example 2 could not be prepared using toluene as a solvent, because coacervation did not occur. These results strongly suggest that the tetramethyleneglycol moieties in Example 6 of the patent application play an important role in the immobilization of $\text{Sc}(\text{OTf})_3$.

13. Evaluation of the three catalysts. Duplicate Mukaiyama aldol reactions were conducted using the polymer incarcerated scandium of the invention (Example 6 from the patent application), and each of Comparative Examples 1 and 2. The amount of Sc leached into the solution was evaluated in each case. The results are shown in Table 1.

[Table 1]



Example (Sc catalyst)	Yield (%)	Leaching of Sc (%)
Example 6 of the patent application	92	ND (<0.05)
Comparative Example 1	55	4.1
Comparative Example 2	85	12.6

When a polymer-incarcerated scandium catalyst of the invention was used (patent example 6), no measureable Sc leaching was observed. However, significant scandium leaching was observed in the case of each of the Comparative Examples. In addition, yield

was significantly higher for Example 6 (of the invention) compared with either of the comparative examples. Comparative Example 1, which uses a polymer like polymer 1c of my JACS 2003 article, provides a yield of only 55%, compared to 92% with the invention of this patent application, and also exhibits significant leaching.

I hereby declare that all statements made in this declaration are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 USC §1001, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Ryo Akiyama
Ryo AKIYAMA

2008. 4. 23
(Date)